

Evaluation of autologous platelet concentrate for intertransverse lumbar fusion

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Abstract

Introduction The aim of the study was to analyze if the adding of autologous platelet concentrate (APC) to a mixture of local autograft plus tricalcium phosphate and hidroxiapatite (TCP/HA) would improve the fusion rate in posterolateral lumbar fusion.

Materials and methods A prospective, controlled, blinded, non-randomized clinical trial was carried out in 107 patients affected by degenerative lumbar pathology. The study group consisted of 67 patients, in which autologous platelet concentration was added to a mixture of autologous local bone graft and TCP/HA. A control group of 40 patients with same pathology and surgical technique but without APC addition was used to compare the fusion mass obtained. By means of plain X-rays, a blinded evaluation of the intertransverse fusion mass quality at twelve and twenty-four months was made according to type A (bilateral uniform mass), type B (unilateral uniform mass) and type C (irregular or lack bilateral mass). Patients with type C were regarded as pseudoarthrosis.

Results In the study group 17 patients had lack or irregular fusion mass (25.4%) versus three patients in the control group (7.5%), which was statistically significant.

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Conclusions This study shows that the adding of autologous platelet concentration to a mixture of autologous bone graft plus TCP/HA has decreased our rates of posterolateral lumbar fusion.

Keywords Autologous platelet concentrate · Growth factors · Spinal fusion · Bone substitutes · Osteoinduction

Introduction

It is well documented that fusion rates in lumbar vertebral surgery have increased after the systematization of pedicular instrumentation. Although results vary depending on different authors, we can consider an 8% average of pseudoarthrosis when posterolateral fusion is performed and 4% when circumferential arthrodesis is done [11]. The autograft which was used by most authors comes from the iliac crest. The morbidity derived from bone harvesting is well known [13, 25].

Trying to avoid the problems derived from bone harvesting, different areas of investigation have been developed, which basically follow two ways: bone substitutors (BS) or promoting substances of bone fusion (FPM). Up to date, different variants of tricalcium phosphate plus hidroxiapatite (TCP/HA) and demineralized bone matrix (DBM) are available for surgeons and at least, for TCP/HA, its usefulness has been demonstrated [9, 19, 25].

The controversy appears when the use of the different bone substitutors can, at its best, get fusion rates, similar to the ones mentioned before. The reason for this is that this kind of products are basically osteoconductors and their osteoinductive capacity does not exist in TCP/HA and creates serious doubts about DBMs. Bone morphogenetic proteins (BMPs) are considered to be the gold standard of

promoting substances of bone fusion. Its commercial availability, for about one decade, has allowed surgeons to work with a demonstrated osteoinductive product [3]. The existence of collateral effects in its intersomatic use and especially its high cost, have limited its use to a very little amount of patients in our country [27].

The big amount of growth factors, which are released in the process of platelet degranulation has opened a new way of work, based on its possible use as FPM. Experience has demonstrated its beneficial effects on soft tissue lesions both if injected or added to the surgical act. The possible beneficial ones on bone pathology are more arguable and literature is scarce and contradictory in results when it's used in lumbar arthrodesis [1, 2, 8, 26, 28].

Since 2002 fusion lumbar surgery has been made in our spine unit using local autograft plus a mixture of TCP/HA because we have checked this has the same fusion rates as using only autograft, avoiding the iliac crest harvesting [19, 20]. The target of our work has been devoted to check if the addition of an autologous platelet concentrate (APC) to local autograft plus TCP/HA was able to increase our rates of posterolateral lumbar fusion.

Materials and methods

This was a prospective, controlled, non-randomized clinical trial. The study was approved by our institutional review board and all patients signed an informed consent. All the patients included in the study were operated to get an intertransverse posterolateral fusion using rigid transpedicular titanium instrumentation, adjoining the accurate neurosurgical acts in relation with their pathology.

The inclusion criteria for this study were patients with lumbar degenerative pathologies after a conservative failing treatment, which was done at least for 12 months.

The exclusion criteria includes lumbar spinal infection, spinal trauma, more than three levels affected, endocrine system diseases (hyperparathyroidism, hyper-hypothyroidism and chronic use of corticosteroids), or instability of tumoral origin.

One hundred and seven patients were studied, who fulfilled inclusion criteria and were operated by the same surgical team using the same kind of vertebral instrumentation. The same surgical technique was used: the facet joints (on their lateral side), pars interarticularis and the transverse processes in the area of instrumentation were meticulously cleaned from soft tissues and decorticated to increase the host area for intertransverse fusion. Removal of the articular cartilage of the facet joints at the levels of fusion was added.

In the study group, 67 consecutively-operated patients were included, for whom, in order to get intertransverse

posterolateral fusion, autologous bone graft was provided, locally harvested from the decompressive site and morselized into small corticocancellous pieces, mixed with TCP/HA and adding autologous platelet concentrate (5 cc for each operated level). No graft from iliac crest was used.

The TCP/HA used in the study was a porous ceramic compound composed of a 40/60 TCP/HA (BCP-BiCalPhos®). Total macroporosity is $80 \pm 10\%$ with macropore size of 400–600 μm and interconnection pore size of 100–150 μm . One 10 cc granules flask was used per fusion level.

Autologous platelet concentrate harvesting was made by taking 100 cc blood during the induction of general anaesthesia. In a close circuit, a processor made the necessary centrifugation until obtaining the final product. Preoperative analytical controls allowed us to check that platelet concentration was always superior to $1.000.000/\text{mm}^3$.

The previous mixture of autograft and bone substitutors was placed in both intertransverse places and we sprayed the obtained autologous platelet concentrate over it. In the system we used, platelets were provided in a fibrin carrier which, at least theoretically, allowed a slower release.

A control group comprised 40 patients with the same inclusion and exclusion criteria and without any differences with the study group in their preoperative characteristics (Table 1), who were operated consecutively by the same team and with the same technique and instrumentation, but for the fact that APC was not added to the local autograft and TCP/HA mixture.

Prophylactic antibiotics were intravenously given for 24 h. The drain was removed on the second day postoperatively. Patients were mobilized two days postop without lumbar brace.

Patients were assessed with radiological techniques (plain roentgenograms) in standing antero-posterior and lateral views. Although conventional radiographic follow-up was done at 0, 3, 6, 12, and 24 months, only the 12-and 24-month AP plain films were used to evaluate the fusion mass in order to carry out the statistical study. The radiological evaluation of the posterolateral fusion on the plain roentgenograms was done by two of the authors as independent observers. Both were blinded to the group of the patients and they used the following simple classification:

Type A: Bilateral, uniform and continuous intertransverse mass (Fig. 1)

Type B: Unilateral uniform and continuous intertransverse mass with discontinuous, irregular or absent intertransverse counterlateral mass (Fig. 2)

Type C: Discontinuous, irregular or absent bilateral intertransverse mass (Fig. 3).

To facilitate the comparative analysis between the two groups, types A and/or B were considered as correct fusion and type C, as no fusion or pseudoarthrosis.

Table 1 Preoperative characteristics of both groups

	“Experimental group” autograft + TCP/HA + APC	“Control group” autograft + TCP/HA
No. of patients	67	40
Age (average)	57	59
Male/female	29/38	24/16
Fusion levels		
L4-L5	22 (32.8%)	15 (37.5%)
L5-S1	12 (18.0%)	9 (22.5%)
L3-L4-L5	11 (16.4%)	7 (17.5%)
L4-L5-S1	22 (32.8%)	5 (12.5%)
L3-L4-L5-S1	0	3 (7.5%)
L3-L4	0	1 (2.5%)

TCP, TriCalcium Phosphate;
HA, HidroxiApatite; APC,
Autologous Platelet Concentrate

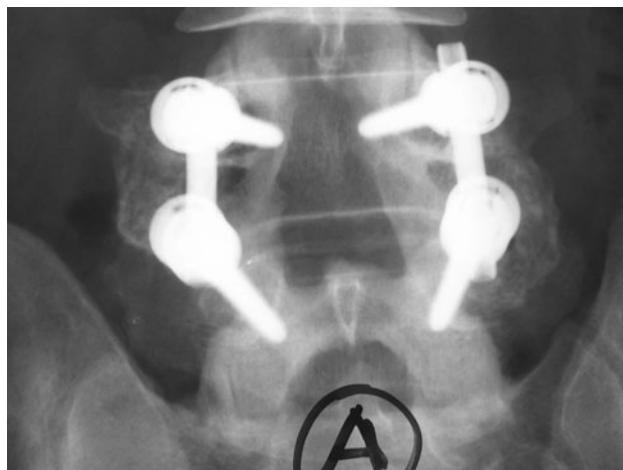


Fig. 1 Type A (bilateral, uniform and continuous intertransverse mass)

For clinical follow-up, the “last observation carried forward” principle was applied but, for the study, only the making of revision surgery by means of painful pseudoarthrosis has been taking into account.

Statistical analysis between groups was performed using Chi square and values of $p < 0.05$ were considered significant. The kappa (κ) test was used to determine interobserver agreement. According to JL Fleiss’s recommendations, the value of kappa exceeding 0.75 represents excellent agreement, values between 0.4–0.75 indicate fair-to-good agreement and values < 0.4 indicate poor agreement.

Results

There was no difference between the X-ray evaluation after both 1 and 2 years, with exactly the same values.

Interobserver agreement expressed by the kappa coefficient was 0.80.

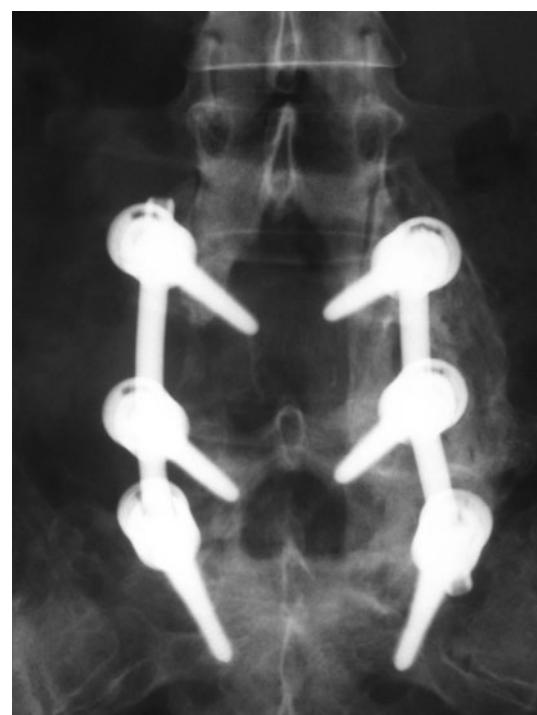


Fig. 2 Type B (unilateral uniform and continuous intertransverse mass with discontinuous, irregular or absent intertransverse contralateral mass)

In the control group (40 patients operated using autologous bone graft and TCP/HA), bilateral fusion mass (type A) was observed in 29 patients (72.5%), unilateral fusion mass (type B) in eight patients (20%) and lack or irregular fusion mass (type C) in three patients (7.5%). Hence, correct fusion was seen in 92.5% of the cases and no fusion in 7.5% (Tables 2, 3).

In the study group (67 patients operated using autologous bone graft, TCP/HA and APC) bilateral fusion mass (type A) was observed in 29 patients (43.3%), unilateral fusion mass (type B) in 21 patients (31.3%) and lack or irregular fusion mass (type C) in 17 patients (25.4%).



Fig. 3 Type C (discontinuous, irregular or absent bilateral inter-transverse mass)

Hence, correct fusion was seen in 74.6% of the cases and no fusion in 25.4%.

Hence, in the study group we got fusion rates which were significantly inferior to those in the control group (74.6 vs. 92.5%, $p = 0.021$ Chi Square test). When we compare, in both groups, the number of patients with mass type A (bilateral uniform), differences are highly significant (72.5 vs. 43.3%, $p = 0.003$ Chi Square test).

There were no local complications, infection, neurologic deficits or broken screws.

At the time of writing this article, we had reoperated 11 out of 20 patients with lack or irregular fusion mass (type C), two from the control group and nine from the study group.

Table 2 Results depending on the obtained fusion mass type

	Bilateral fusion mass (type A)	Unilateral fusion mass (type B)	Lack or irregular fusion mass (type C)
“Experimental group” autograft + TCP/HA + APC	43.3% (29)	31.3% (21)	25.4% (17)
“Control group” autograft + TCP/HA	72.5% (29)	20% (8)	7.5% (3)
$p = 0.003$			

TCP, Tricalcium phosphate; HA, Hidroxiapatite; APC, Autologous platelet concentrate

Table 3 Results depending on correct fusion or not (pseudoarthrosis)

	Correct fusion (type A or type B)	No fusion = pseudoarthrosis (type C)
“Experimental group” autograft + TCP/HA + APC	74.6% (50)	25.4% (17)
“Control group” autograft + TCP/HA	92.5% (37)	7.5% (3)
$p = 0.021$		

TCP, Tricalcium phosphate; HA, Hidroxiapatite; APC, Autologous platelet concentrate

Discussion

It is known that in the flow of chemicals steps produced in a fracture healing, platelets degranulation releases a group of proteins, generically known as autologous growth factors. Inside, platelets have three types of granules. The so-called alpha-granules contain more than 30 bioactive proteins, many of which have a fundamental role in haemostasis and tissue healing. The platelet-derived growth factor (PDGF), the insulin-like growth factor (IGF), the transforming growth (TGF) and the vascular endothelial growth factor (VEGF) are some of these proteins.

After platelets have been collected, nowadays, thanks to specific instruments, they start to release the above mentioned factors in a short time. Theoretically, these proteins would stimulate the proliferation and differentiation of mesenchymal stem cells and would facilitate bone formation behaving as histopromotive factors [1, 7]. Platelet concentration harvesting is simple, safe, not too dear and causes little discomfort to the patient. Its autologous origin avoids immunologic reactions and disease transmission.

It has been suggested that at least five times the amount of platelets/mm³ in peripheral blood is necessary in the autologous platelet concentrate to be effective. It is also known that 95% of the factors are released within the first hour, although platelets synthesize and secrete new factors during several days once the autologous platelet concentrate has been installed over the tissue to heal [1].

On this evidence, it was reported that the use of autologous growth factors theoretical strength could be used in a lot of fields of restorative medicine. Hence, progressively, it has been used in plastic surgery (skin injuries in diabetic patients, decubitus ulcers...), odontology (filling of

periodontal lysis...), sports medicine (muscular-tendon repair, tennis elbow, ligament tears..). The initial results, yet promising, lack conclusive scientific evidence, which would allow to encourage its general application [1, 2, 8, 10, 16, 18, 21, 23].

Starting from this previous experience, animal control studies were designed to learn if adding APC to autografts and/or bone substitutes would achieve the improvement of fusion mass (quality and rates) in posterolateral or circumferential arthrodesis in the lumbar segment. The results, although irregular, don't improve the ones obtained when autograft is used [1, 15, 22]. The clinical experience is even more contradictory. Its use in intersomatic arthrodesis shows similar results between autograft or allograft plus autologous platelet concentrate [14]. When the analysis of the cage filled with autograft (with or without autologous platelet concentrate) was made by CT, it was observed a quicker fusion in those patients with autologous platelet concentrate added, although the result, at the end of the follow-up, was the same [12]. It is true some authors emphasize on its goodness for lumbar arthrodesis [4, 6] but our results agree with those from literature and we can claim, as a rule, that we get less fusion rates when adding autologous platelet concentrate to autograft or autograft plus TCP/HA [5, 17, 24, 26, 30]. So far, all clinical reports are case studies and we did not find level-1 data to support the use of autologous platelet concentrate in spinal fusion [1].

Although there are no epidemiologic differences between groups, our study, yet prospective, is non-randomized. Local autograft amount and quality is not uniform although this fact lies in both groups. Both facts mean some limitations to the study which has been carried out.

Although the literature support is really scarce, to explain our results, we can suggest some hypothesis. Individual variability avoids exactly knowing the amount and quality of autologous growth factors in the platelet concentration harvest [29]. It is possible that spray-like adding would not be the ideal way and it would be necessary to design an adequate carrier different from the fibrine we used in our trial. The same growth factor can act as a promotor or inhibitor, depending on the way of releasing and the environment conditions where they are kept [1]. Theoretically, it is possible that TCP/HA presence can mean a negative aspect after “loosing” part of autologous platelet concentrate in an osteoconductive material. We need more randomized studies, including a bigger sample, to check if our data can be kept or a new methodology may be used.

Conclusion

In our experience, we have not been able to prove if the adding of autologous platelet concentration to a mixture of

autologous bone graft plus TCP/HA would increase the rates of posterolateral lumbar fusion and even, rates have decreased in this study.

Conflict of interest None.

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